Porcine neural xenografts in rats and mice: donor tissue development and characteristics of rejection.

Larsson LC, Frielingsdorf H, Mirza B, Hansson SJ, Anderson P, Czech KA, Strandberg M, Widner H.

Section for Neuronal Survival, Department of Physiological Sciences, Wallenburg Neuroscience Center, Lund University, SE-221 84 Lund, Sweden. Lena.Larsson@mphy.lu.se

Embryonic ventral mesencephalic tissue from the pig is a potential alternative donor tissue for neural transplantation to Parkinson's disease patients. For stable graft survival, the host immune response has to be prevented. This study was performed in order to analyze the mechanisms and dynamics of neural xenograft rejection, as well as neurobiological properties of the donor tissue. Adult normal mice and rats, and cyclosporin A-treated rats, received intrastriatal transplants of dissociated embryonic ventral mesencephalic pig tissue that was 27 or 29 embryonic days of age (E27 and E29). The animals were perfused at 2, 4, 6, and 12 weeks after grafting and the brains were processed for immunohistochemistry of dopaminergic (tyrosine hydroxylase positive) neurons, CD4(+) and CD8(+) lymphocytes, natural killer cells, macrophages, microglia, and astrocytes. Thirty-five rats received daily injections of BrdU for 5 consecutive days at different time points after transplantation and were perfused at 6 weeks. These animals were analyzed for proliferation of cells in the donor tissue, both in healthy and in rejecting grafts. No tyrosine hydroxylase-positive cells proliferated after grafting. Our results demonstrated that E27 was superior to E29 donor tissue for neurobiological reasons. Cyclosporin A immunosuppression was protective only during the first weeks and failed to protect the grafts in a long-term perspective. Grafts in mice were invariably rejected between 2 and 4 weeks after transplantation, while occasional grafts in untreated rats survived up to 12 weeks without signs of an ongoing rejection process. CD8(+) lymphocytes and microglia cells are most likely important effector cells in the late, cyclosporin A-resistant rejection process.

PMID: 11681844 [PubMed - indexed for MEDLINE]